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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/996,484	11/28/2001	Yen Choo	8325-2008	2713

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EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	PAPER NUMBER
1636	

MAIL DATE	DELIVERY MODE
11/09/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/996,484	CHOO ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 September 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,7,8,10,11,13-15,21-26,31,34,35,38-47 and 50-54* is/are pending in the application.

4a) Of the above claim(s) *1,2,4,5,7,8,10,11,13-15,21-26,31,35 and 38-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34 and 50-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after a decision by the Board of Patent Appeals and Interferences, but before the filing of a Notice of Appeal to the Court of Appeals for the Federal Circuit or the commencement of a civil action. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 9/1/2010 has been entered.

Receipt is acknowledged of an amendment, filed 9/1/2010, in which claim 48 was canceled, claim 34 was amended, and claims 50-54 were newly added. Claims 1, 2, 4, 5, 7, 8, 10, 11, 13-15, 21-26, 31, 34, 35, 38-47 and 50-54 are pending.

Election/Restrictions

Applicant elected Group III without traverse in the reply filed 4/16/2004.

Claims 1, 2, 4, 5, 7, 8, 10, 11, 13-15, 21-26, 31, 35 and 38-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/16/2004.

Claims 34 and 50-54 are under consideration.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 120, a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference **must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications**.

If the instant application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an

unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

In the instant case, the transmittal form filed on the filing date of the present application requests the amendment of the specification to state the following:

--Cross Reference to Related Applications

This applications claims priority under 35 U.S.C. §365(c) and 35 U.S.C. §120 to PCT/GB00/02080 and priority under 35 U.S.C. § 119/363 to United Kingdom applications serial nos. 9912635.1 and 0001582.6.--

This reference does not provide the relationship between the present application and PCT/GB00/02080.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 52-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The preamble of claims 52-54 is directed to a "protein switch." The present specification defines "protein switch" to "describe a multiple component system comprising (i) a first polypeptide molecule; (ii) a second polypeptide molecule which binds to the first polypeptide molecule in a manner modulated by a ligand; and (iii) the ligand" (page 10, lines 30-32). However, the components of the "protein switch" required by claims 52-54 are (i) a polypeptide comprising an engineered, non-naturally occurring Cys2-His2 zinc finger binding domain that binds to a target site in DNA; and (ii) a ligand, wherein binding of the zinc finger binding domain to the target site is modulated in the presence of the ligand. Thus, the claims are directed to a "protein switch" where the ligand modulates the binding of two polypeptides, yet the body of the claims set forth a ligand that modulates binding of a polypeptide to DNA. It would be remedial to amend the preamble to remove the reference to the "protein switch" since the elements of a protein switch are not recited in the body of the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 34, 51, 52 and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Corbi et al (FEBS Letters, Vol. 471, pages 71-74, 1997; see the entire reference). This is a new rejection.

Corbi et al teach an engineered, non-naturally occurring zinc finger polypeptide named "Mago", which is able to bind the "code" predicted DNA sequence 5'-ATG TGG GTT-3' (e.g., page 71, paragraph bridging columns; sections 2.1, 3.1 and 3.2). Corbi et al teach the "Mago" polypeptide bound to unlabeled DNA target probe 5'-ATG TGG GTT-3' (ligand), where "Mago" becomes dissociated from the target site in the labeled DNA when "Mago" is bound to is the unlabeled DNA target probe (ligand) (e.g., sections 2.2 and 3.2; Figure 2).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 34, 50, 52 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Christopherson et al (Proceedings of the National Academy of Sciences USA, Vol. 89, No. 14, pages 6314-6318, July 1992; see the entire reference) in view of Choo et al (WO 98/53059; see the entire reference). This is a new rejection.

Christopherson et al teach a complex comprising a polypeptide comprising (i) a DNA binding domain and an ecdysone receptor ligand binding domain; and (ii) a ligand, such as muristerone A, that binds to the ligand binding domain (e.g., pages 6314-6315, Materials and Methods; pages 6315-6317, Results; Figure 2). Christopherson et al teach the polypeptide where the DNA binding domain is selected from a wild type ecdysone receptor DNA binding domain, a glucocorticoid receptor DNA binding domain, an engineered, non-naturally occurring rat glucocorticoid receptor DNA binding domain containing a two-amino acid substitution (G458E, S459G) that alters the DNA-binding specificity; and an *E. coli* LexA DNA binding domain (e.g., Figure 2). Christopherson et al teach that each of the DNA-binding and transactivation activities of these proteins were rendered ecdysteroid-dependent when fused to the ligand-binding domain of the ecdysone receptor (e.g., Abstract; pages 6315-6317, Results; Tables 1-2). Christopherson

et al teach that novel target-gene specificity was obtained by using the chimeric receptors containing the ecdysone receptor ligand-binding domain fused to heterologous DNA binding domains (e.g., page 6314, paragraph bridging columns; paragraph bridging pages 6317-6318). Further, the transcriptional regulatory activities of the fusion polypeptides are dependent upon the addition of exogenous ligand, allowing one to "switch on" the activator with ecdysteroids (e.g., paragraph bridging pages 6317-6318; page 6318, left column, 2nd full paragraph). Christopherson et al teach that the development of a system for regulated expression of endogenous and exogenous genes in eukaryotic cells should provide an important method to study the function of those gene products (e.g., page 6318, left column, 2nd full paragraph).

Christopherson et al do not teach the complex where the engineered, non-naturally occurring DNA binding domain is an engineered, non-naturally occurring Cys2-His2 zinc finger DNA binding domain.

Choo et al teach that protein-nucleic acid recognition is a commonplace phenomenon which is central to a large number of biomolecular control mechanisms which regulate the function of eukaryotic and prokaryotic cells, such as the regulation of gene expression (e.g., page 1, lines 7-11). Choo et al teach a code which permits the selection of any nucleic acid sequence as the target sequence for the design of a specific zinc finger nucleic acid-binding protein which will bind thereto (e.g., paragraph bridging pages 2-3). Choo et al teach that the zinc finger nucleic acid-binding protein is a protein of the Cys2-His2 zinc finger class capable of binding to a nucleic acid base triplet in a target nucleic acid sequence, wherein binding to the nucleic acid base triplet by an alpha-helical zinc finger nucleic acid protein is determined according to the disclosed code (e.g., page 3, line 6-27; page 6, line 21 to page 7, line 12). Thus, Choo et al teach

a polypeptide comprising an engineered, non-naturally occurring Cys2-His2 zinc finger binding domain, the zinc finger binding domain capable of binding to a DNA target site. Further, Choo et al teach that the disclosed zinc finger binding motifs can be combined into nucleic acid binding proteins having a multiplicity of fingers, commonly at least three zinc fingers (e.g., page 13, lines 6-22). Choo et al teach that the invention provides nucleic acid binding proteins which can be engineered with exquisite specificity, lending to the design of any zinc finger-comprising molecule of which specific nucleic acid binding is required (e.g., page 25).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to replace the engineered, non-naturally occurring DNA binding domain of Christopherson et al with an engineered, non-naturally occurring Cys2-His2 zinc finger binding domain taught by Choo et al because Christopherson et al teach it is within the ordinary skill in the replace the wild type ecdysone receptor DNA binding domain with a heterologous domain, including one mutated to provide altered DNA-biding specificity, and Choo et al teach engineered, non-naturally occurring Cys2-His2 zinc finger binding domains designed by the disclosed rules to bind to any particular target sequence.

One would have been motivated to make such a modification in order to receive the expected benefit of providing polypeptides whose DNA-binding and transactivation activity are regulated by an exogenous ligand as taught by Christopherson for the regulation of any gene targeted by the engineered, non-naturally occurring Cys2-His2 zinc finger DNA binding domain of Choo et al. By altering the DNA binding specificity one would provide a system for regulated expression of endogenous and exogenous genes in eukaryotic cells to provide an important method to study the function of those gene products. Based upon the teachings of the cited

references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 52 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lim et al (US Patent No. 7,189,506 B1; see the entire reference) in view of Choo et al (WO 98/53059; see the entire reference). This is a new rejection.

Lim et al teach a molecular switch system comprising a transcriptional regulatory polypeptide and an exogenously supplied compound, which targets nucleic acid, not protein (e.g., column 14, lines 50-59). Lim et al teach that the compound, when bound to double stranded DNA at sites in the vicinity of regulatory protein binding sequences, can displace the bound protein (e.g., column 14, lines 50-59). Lim et al teach a transcriptional regulatory fusion protein which is a recombinant fusion protein consisting essentially of a DNA binding domain and a regulatory domain, where the regulatory protein is (1) natural (native), (2) chimeric (chimera of the DNA-binding domain of a natural protein and the regulatory (activator or repressor) domain of a natural protein, (3) synthetic, having a novel DNA-binding domain designed by structural modeling, phage display screen, or other methods, or (4) may not take the form of a fusion protein (e.g., column 9, line 55 to column 10, line 4; column 12, lines 28-52; column 15, lines 1-14). With regard to synthetic transcriptional regulatory fusion proteins, Lim et al teach that the protein may be engineered or designed to specifically bind a compound-binding sequence/transcriptional regulatory binding site, such as novel zinc three-finger proteins which bind to a specific 9 to 10 bp sequence (e.g., column 16, line 30 to column 17, line 2).

Lim et al do not specifically teach that the engineered, non-naturally occurring zinc finger binding domains are Cys2-His2 zinc finger binding domains.

Choo et al teach that protein-nucleic acid recognition is a commonplace phenomenon which is central to a large number of biomolecular control mechanisms which regulate the function of eukaryotic and prokaryotic cells, such as the regulation of gene expression (e.g., page 1, lines 7-11). Choo et al teach a code which permits the selection of any nucleic acid sequence as the target sequence for the design of a specific zinc finger nucleic acid-binding protein which will bind thereto (e.g., paragraph bridging pages 2-3). Choo et al teach that the zinc finger nucleic acid-binding protein is a protein of the Cys2-His2 zinc finger class capable of binding to a nucleic acid base triplet in a target nucleic acid sequence, wherein binding to the 5' base of the nucleic acid base triplet by an alpha-helical zinc finger nucleic acid protein is determined according to the disclosed code (e.g., page 3, line 6-27; page 6, line 21 to page 7, line 12). Thus, Choo et al teach a polypeptide comprising an engineered, non-naturally occurring Cys2-His2 zinc finger binding domain, the zinc finger binding domain capable of binding to a DNA target site. Further, Choo et al teach that the disclosed zinc finger binding motifs can be combined into nucleic acid binding proteins having a multiplicity of fingers, commonly at least three zinc fingers (e.g., page 13, lines 6-22). Choo et al teach that the invention provides nucleic acid binding proteins which can be engineered with exquisite specificity, lending to the design of any zinc finger-comprising molecule of which specific nucleic acid binding is required (e.g., page 25).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the polypeptide of the molecular switch system of Lim et al to specifically

include the engineered, non-naturally occurring Cys2-His2 zinc finger binding domains taught by Choo et al as the non-naturally occurring zinc finger binding domain of the transcriptional regulatory polypeptide because Lim et al teach it is within the ordinary skill in the art to use engineered, non-naturally occurring zinc finger binding domains and Choo et al teach that it is the Cys2-His2 zinc finger class that is capable of being engineered to bind a particular sequence according to the disclosed code.

One would have been motivated to make such a modification in order to receive the expected benefit of providing a transcriptional regulatory polypeptide capable of binding a particular target binding site with specificity as taught by Choo et al. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Arguments - 35 USC § 103

The rejection of claims 34 and 48 under 35 U.S.C. 103(a) as being unpatentable over Gilman et al (WO 96/06110) has been withdrawn in view of Applicant's amendment to the claims in the reply filed 9/1/2010.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is (571)272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Dunston/
Primary Examiner
Art Unit 1636